AMENDMENTS TO THE SPECIFICATION

Please replace the last paragraph on page 54 as follows:

GPA_{ID} and GPA_{LW} hybrids. The regions of high homology among Gα subunits that have been identified by sequence alignment are interspersed throughout the molecule. The G1 region containing the highly conserved –GSGESGDST- (SEQ ID NO:127) motif is followed immediately by a region of very low sequence ~~consevation~~ conservation, the "i1" or insert 1 region. Both sequence and length vary considerably among the i1 regions of the Gα subunits. By aligning the sequences of Gα subunits, the conserved regions bounding the i1 region were identified and two additional classes of GPA1-Gα hybrids were constructed. The GPA_{ID} hybrids encode the amino terminal 102 residues of GPA1 (up to the sequence -QARKLGIQ- (SEQ ID NO:122)) fused in frame to mammalian Gα subunits, while the GPA_{LW} hybrids encode the amino terminal 244 residues of GPA1 (up to the sequence -LIHEDIAKA- (SEQ ID NO:123) in GPA1). The reason for constructing the GPA_{ID} and GPA_{LW} hybrids was to test the hypothesis that the i1 region of GPA1is required for mediating the interaction of GPA1 with yeast Gβγ subunits, for the stable expression of the hybrid molecules, or for function of the hybrid molecules. The GPA_{ID} hybrids contain the amino terminal domain of GPA1 fused to the i1 domain of mammalian subunits, and therefore do not contain the GPA1 i1 region, while the GPA_{LW} hybrids contain the amino terminal 244 residues of GPA1 including the entire i1 region (as defined by sequence alignments). Hybrids of both GPA_{ID} and GPA_{LW} classes were constructed for GαS, Gαi2, Gαi3, $G\alpha o_a$, and Gα16; none of these hybrids complemented the *gpa1* growth arrest phenotype.

Please replace the last paragraph on page 55 and the first paragraph on page 56 as follows:

Gαs Hybrids. There is evidence that the "switch region" encoded by residues 171-237 of Gα transducin (using the numbering of Noel et al (1993)) also plays a role in Gβγ coupling. First, the G226A mutation in GαS (Miller et al. 1988) prevents the GTP-induced conformational change that occurs with exchange of GDP for GTP upon receptor activation by ligand. This residue maps to the highly conserved sequence -DVGGQ- (SEQ ID NO:128), present in all Gα subunits and is involved in GTP hydrolysis. In both the Gαt and Gαi1 crystal structures, this sequence motif resides in the loop that connects the_β3 sheet and the α 2 helix in the guanine nucleotide binding core. In addition to blocking the conformational change that occurs upon GTP binding, this mutation also prevents dissociation of GTP-liganded Gαs from Gβγ. Second, crosslinking data reveals that a highly conserved cysteine residue in the α2 helix (C215 in Gαo, C210 in Gαt) can be crosslinked to the carboxy terminal region of Gβ_subunits. Finally, genetic evidence (Whiteway et al. 1993) identifies an important single residue in GPA1 (E307) in the β2 sheet of the core structure that may be in direct contact with βγ. A mutation in the GPA1 protein at this position suppresses the constitutive signalling phenotype of a variety of STE4 (Gβ) dominant negative mutations that are also known to be defective in Gα-Gβγ association (as assessed in two-hybrid assay in yeast as well as by more conventional genetic tests).

Please replace the paragraph in the middle of page 98 as follows:

Clearly, these sequences encode novel peptides, as the native a-factor sequence differs considerably:

Tyr Ile Ile Lys Gly Val Phe Trp Asp Pro Ala (SEQ ID NO:129).

Please replace the full paragraph on page 110 as follows:

A hybrid gene encoding the prepro-region of human POMC (accession # K02406; Takahashi, H., et al (1983) Nucleic Acids Research 11:6847-6858) and the coding region of a single repeat of mature α-factor will be constructed in the following fashion. The prepro-region of human POMC will be amplified with an HindIII site at the 5' end and a BbsI site at the 3' end using VENT polymerase and the following primers: 5' GGGAAGCTT ***ATG***CCGAGATCGTGCTGCCAGCCGC 3' (SEQ ID NO:30) (HindIII site is underlined and initiation codon is italic bold) and antisense 5' GGGGAAGACTTCTGCCCTGCGCCGCTGCTGCC 3' (SEQ ID NO:31) (BbsI recognition is underlined), leaving the amino acid sequence -SSGAGQ**KR**- (SEQ ID NO:125) at the 3' end with a Bbs1 site leaving an overhang at the -KR- dibasic cleavage sequence. The coding region of α-factor will be amplified from Cadus 1219 with a Bbs1 site at the 5' end and a BglII site at the 3' end using the primers 5' GGGGAAGACCCGCAGGAGGCAGAAGCTT GGTTGCAG 3' (SEQ ID NO:32) (BbsI site is underlined) and 5' GGGAGATCT**TCA**GTACATTGGTTGGCC 3' (SEQ ID NO:33) (BglII site is underlined, termination codon is bold). The PCR fragment encoding the pre-pro segment of POMC is restricted with HindIII and BbsI and gel purifed, the PCR fragment encoding α-factor is cut with BbsI and BglII and gel purified, and Cadus 1215 is cut with BglII and partially with HindIII and the HindIII-BglII restricted vector containing the pAlter polylinker sequences is gel purified. Three-part ligation of the two PCR products with HindIII and BglII digested Cadus 1215 will yield a hybrid POMC/α-factor gene in which the first 104 amino acids residues are from POMC and the remaining 17 are from α-factor. The structure of this hybrid gene around the PC1 cleavage site is: –RNSSSSGSSGAGQ**KR**EAEA*WHWLQLKPGQPMY** (SEQ ID NO:34) where residues donated by POMC are underlined, the dibasic cleavage site is underlined bold, and the sequence of mature α-factor is in italics. The tetrapeptide -EAEA- (SEQ ID NO:130) juxtaposed between the dibasic cleavage site and the amino-terminal tryptophan of mature α-factor should be removed by the dipeptidyl aminopeptidase activity of ste13p.

Please replace the first line of Table 7 on page 153 as follows:

GPA1 RIDTTGITETEFNIGSSKFKVLDAGGQRSERKKWIHCFEGITAV LFVLAMSEYDQMLFEDER (SEQ ID NO:131)